CLAIMS

1. A biocompatible fluid adhesive protein foam, which is bioresorbable and nontoxic, for surgical and/or therapeutic use, in particular for protecting/cicatrizing tissue wounds and for attaching biological tissues to each other or to an implanted biomaterial, characterized in that it comprises a biocompatible fluid adhesive protein matrix, which is bioresorbable and nontoxic, containing a biocompatible and nontoxic gas or mixture of gases.

2. The adhesive foam as claimed in claim 1, characterized in that the adhesive matrix consists of, or comprises, an at least partially polymerized/crosslinked protein compound which is nontoxic, biocompatible and biodegradable and which has adhesive properties, said protein compound optionally being chemically modified.

3. The adhesive foam as claimed in either of claims 1 and 2, characterized in that the protein compound consists of, or comprises, a protein or a mixture of proteins selected from collagen, gelatin, albumin, elastin and fibrinogen, preferably from collagen and albumin.

4. The adhesive foam as claimed in any one of claims 1 to 3, characterized in that the protein compound consists of, or comprises, collagen.

5. The adhesive foam as claimed in claim 4, characterized in that the protein compound consists of, or comprises, native collagen, native collagen which is chemically modified, especially by methylation, by succinylation or by oxidative cleavage in particular with the aid of periodic acid or a salt thereof, native collagen without telopeptides or nonhydrolyzed collagen which has at least partially lost its helical structure, consisting mainly of α chains the molecular weight of which is close to 100 kDa (heated collagen).

6. The adhesive foam as claimed in claim 4, characterized in that the protein compound consists of, or comprises, heated collagen.

7. The adhesive foam as claimed in any one of claims 1 to 6, characterized in that the protein compound is crosslinked with a reactive polymer of molecular weight higher than 1000, preferably selected from macromolecular polyaldehydes and hydrophilic polymers capable of reacting with the protein compound, in particular with respect to amine or sulfhydryl functions.

8. The adhesive foam as claimed in claim 7, characterized in that the macromolecular polyaldehyde is selected from oxidized polysaccharides or mucopolysaccharides, preferably from starch, dextran, agarose, cellulose, chitin, chitosan, alginic acid, glycosaminoglycans, hyaluronic acid and chondroitin sulfate, and the derivatives or mixtures thereof, more preferably from starch, dextran and hyaluronic acid.

9. The adhesive foam as claimed in claim 8, characterized in that the macromolecular polyaldehyde comprises oxidized starch.

10. The adhesive foam as claimed in claim 7, characterized in that the hydrophilic polymer is chosen from derivatives of poly(ethylene) glycol (PEG), poly(oxyethylenes), poly(methylene glycols), poly(trimethylene glycols) and poly(vinylpyrrolidones), derivatives of PEG being the most preferred.

11. The adhesive foam as claimed in any one of claims 1 to 9, characterized in that the adhesive matrix consists of, or comprises, heated collagen crosslinked with oxidized starch.

12. The adhesive foam as claimed in any one of claims 1 to 3 and 7 to 9, characterized in that the adhesive matrix consists of, or comprises, albumin crosslinked with oxidized starch.

13. The adhesive foam as claimed in any one of claims 1 to 3, 7 and 12, characterized in that the adhesive matrix consists of, or comprises, albumin crosslinked with a reactive polymer.

14. The adhesive foam as claimed in any one of claims 1 to 3, characterized in that the adhesive matrix consists of, or comprises, a fibrin glue.

15. The adhesive foam as claimed in any one of claims 1 to 14, characterized in that the gas is selected from air, nitrogen, oxygen and carbon dioxide or the mixture of one or more of these gases, preferably from air, carbon dioxide and nitrogen, air being most particularly preferred.

16. The adhesive foam as claimed in any one of claims 1 to 15, characterized in that the volume of gas represents 25 to 90% of the total volume of the foam, preferably 40 to 75%.

17. The adhesive foam as claimed in any one of claims 1 to 16, characterized in that the foam contains one or more biologically active substances.

18. The adhesive foam as claimed in any one of claims 1 to 17, characterized in that it is tightly attached to a collagen film.

~~19.~~ A process for producing a biocompatible fluid adhesive protein foam, which is bioresorbable and nontoxic, for surgical and/or therapeutic use, in particular for protecting/cicatrizing tissue wounds and for attaching biological tissues to each other or to an implanted biomaterial, characterized in that it comprises extemporaneously mixing, in a homogeneous manner, a protein compound which can be polymerized/crosslinked, and which is potentially adhesive, with a polymerization/crosslinking agent so as to form a fluid biocompatible adhesive protein matrix material, which is bioresorbable and nontoxic, and a biocompatible and nontoxic gas or mixture of gases with this fluid adhesive protein matrix material or with one of the basic constituents of such a material solubilized in aqueous medium.

~~24.~~ The process as claimed in claim 19, characterized in that the protein compound in solid form, in particular in the form of fibers or of dry powder, is mixed extemporaneously with a buffered

aqueous solution with the aid of heating means, and in that the polymerization/crosslinking agent is supplied to the mixture.

21. The process as claimed in either of claims 19 and 20, characterized in that the protein compound is as defined in any one of claims 3 to 6.

22. The process as claimed in claim 19, characterized in that the protein compound consists of, or comprises, native collagen in the form of an aqueous solution at a concentration of between 1 and 5%, preferably 2.5 and 4% by weight.

23. The process as claimed in claim 19, characterized in that the protein compound consists of, or comprises, heated collagen solubilized in aqueous medium at a concentration of between 4 and 20%, preferably between 5 and 18% by weight.

24. The process as claimed in either of claims 19 and 21, characterized in that the protein compound consists of, or comprises, albumin solubilized in aqueous medium at a concentration of between 20 and 50%, preferably 40 to 50%.

25. The process as claimed in any one of claims 19 to 24, characterized in that the polymerization/cross-linking agent is a reactive polymer as defined in any one of claims 7 to 10.

26. The process as claimed in claim 25, characterized in that the polymerization/crosslinking agent is a macromolecular polyaldehyde solubilized in aqueous medium at a concentration of between 0.5 and 10% by weight, preferably between 1 and 3% by weight.

27. The process as claimed in any one of claims 19 to 23 and 25 to 26, characterized in that the protein compound consists of, or comprises, native collagen or heated collagen, and the polymerization/crosslinking agent is oxidized starch.

28. The process as claimed in any one of claims 19 to 21, 23 and 26, 27, characterized in that the proportion of macromolecular polyaldehyde to heated

collagen is 1/10 to 1/160, preferably 1/15 to 1/50, the mixing temperature being between 35°C and 41°C.

29. The process as claimed in any one of claims 19 to 22 and 25 to 27, characterized in that the proportion of macromolecular polyaldehyde to native collagen is between 1/10 and 1/50, preferably 1/10 to 1/30, and the mixing temperature is between 18°C and 37°C.

30. The process as claimed in any one of claims 19 to 21, characterized in that the protein compound has been modified chemically or by oxidative cleavage beforehand, in particular by treatment with periodic acid or a salt thereof, and in that the polymerization agent consists of a buffer at slightly alkaline pH so as to allow the polymerization/crosslinking of the protein compound at an approximately neutral pH.

31. The process as claimed in any one of claims 19 to 21, characterized in that it comprises mixing fibrinogen with thrombin, in aqueous solution.

32. The process as claimed in any one of claims 19 to 31, characterized in that the gas is selected from air, nitrogen, oxygen and carbon dioxide or the mixture of one or more of these gases, preferably from air, carbon dioxide and nitrogen, air being most particularly preferred.

33. The process as claimed in any one of claims 19 to 32, characterized in that the gas is combined with one or more of the constituents for the adhesive protein matrix.

34. The process as claimed in any one of claims 19 to 33, characterized in that the gas is combined with a biocompatible and nontoxic vehicle, preferably formed from a protein compound as claimed in claim 21.

35. The process as claimed in any one of claims 19 to 33, characterized in that the gas is supplied with the aid of the polymerization/crosslinking agent and/or of the vehicle in pulverulent or lyophilized form.

36. The process as claimed in any one of claims 19 to 33, characterized in that the gas is supplied with

the aid of the protein compound in pulverulent or lyophilized form.

37. The process as claimed in any one of claims 19 to 36, characterized in that the volume of gas introduced represents 25 to 90% of the total volume of the adhesive foam, preferably 40 to 75%.

38. The process as claimed in any one of claims 19 to 37, characterized in that it comprises introducing one or more biologically active substances into the adhesive protein matrix material.

39. The process as claimed in claim 38, characterized in that the biologically active substance(s) is (are) combined with a biocompatible and nontoxic vehicle which is optionally the vehicle for the gas or the mixture of gases.

40. The process as claimed in any one of claims 19 to 39, characterized in that the adhesive fluid protein foam is produced by transferring the mixture back and forward between two syringes.

41. The process as claimed in any one of claims 19 to 40, characterized in that the gas is introduced into the adhesive matrix material (matrix in the process of forming).

42. The process as claimed in any one of claims 19 to 40, characterized in that the gas is introduced at the time of mixing the constituents for the formation of the adhesive matrix.

43. The process as claimed in any one of claims 19 to 42, characterized in that the gas is mixed with the adhesive matrix material so as to give a temperature of between 18°C and 41°C.

44. A kit for preparing a biocompatible fluid adhesive protein foam, which is bioresorbable and nontoxic, for surgical and/or therapeutic use, in particular for protecting/cicatrizing tissue wounds and attaching biological tissues to each other or an implanted biomaterial, characterized in that it comprises a potentially adhesive protein compound which can be polymerized/crosslinked, solubilized in aqueous

medium, and a polymerization/crosslinking agent, for forming a biocompatible fluid adhesive protein matrix, which is bioresorbable and nontoxic, a biocompatible and nontoxic gas or mixture of gases and means for extemporaneously mixing the constituents, protein compound in aqueous solution and polymerization/crosslinking agent for forming the adhesive matrix, and said gas or mixture of gases.

45. The kit as claimed in claim 44, characterized in that it comprises a first container containing the potentially adhesive protein compound in pulverulent, dehydrated and optionally sterilized form, a second container containing an optionally sterile buffered aqueous solution, means for supplying a polymerization/crosslinking agent to the solubilized protein compound and means for mixing the content of the first and second containers, and means for using a gas in said mixture and producing the foam.

46. The kit as claimed in either of claims 44 and 45, characterized in that the protein compound, the polymerization/crosslinking agent and the gas are as defined in any one of claims 21 to 39.

47. The kit as claimed in claim 44, characterized in that it is in the form of two syringes equipped with mixing means, in which one of the syringes contains the protein compound in aqueous solution and the other contains the polymerization/crosslinking agent.

48. The kit as claimed in any one of claims 44 to 47, characterized in that the gas is combined with the protein compound and/or with the polymerization/crosslinking agent.

49. The kit as claimed in claim 45, characterized in that said mixing means make it possible to pass the mixture from one syringe to the other several times so as to ensure the formation of the foam using the gas included in the syringe containing the pulverulent protein compound.

50. The kit as claimed in any one of claims 44 to 48, characterized in that the gas is combined with a

biocompatible and nontoxic vehicle, preferably formed form a protein compound as claimed in claim 21.

51. The kit as claimed in any one of claims 44 to 48, characterized in that it comprises a third syringe containing the gas optionally combined with a vehicle.

52. The kit as claimed in claim 51, characterized in that the vehicle also contains one or more biologically active substances.

53. The kit as claimed in any one of claims 44 to 52, characterized in that the polymerization/cross-linking agent and/or the vehicle is in lyophilized form.

54. The use of a fluid adhesive protein foam as claimed in any one of claims 1 to 18, for preventing or stopping the bleeding of vascular or tissue wounds, for attaching biological tissues, including live tissues, to each other or to an implanted biomaterial, for cicatrizing surgical or chronic wounds, protecting or sealing sutures, preventing the formation of postoperative adhesions, delivering biologically active substances in particular with medicines for local application and filling tissue cavities (bone, cartilage, skin lesions, etc).